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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/006,352	01/13/1998	REINER GENTZ	PF454	3633

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EXAMINER
O HARA, EILEEN B

ART UNIT	PAPER NUMBER
1646	22

DATE MAILED: 05/30/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/006,352	GENTZ ET AL.	
	Examiner	Art Unit	
	Eileen B. O'Hara	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 March 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-159 and 285-305* is/are pending in the application.

4a) Of the above claim(s) *118-135* is/are withdrawn from consideration.

5)☒ Claim(s) *See Continuation Sheet* is/are allowed.

6)☒ Claim(s) *136,137,148,149,288-292,298 and 302-305* is/are rejected.

7)☒ Claim(s) *31,47,64,79,95,109 and 301* is/are objected to.

8)☒ Claim(s) *24-159 and 285-305* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 March 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11,15,21* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Continuation of Disposition of Claims: Claims allowed are 24-30,32-46,48-63,65-78,80-94,96-108,110-117,138-147,150-159,285-287,293-297,299 and 300.

DETAILED ACTION

1. Claims 24-159 and 285-305 are pending in the instant application. Claims 40, 45, 47, 50, 53-55, 72, 88, 104, 136 and 148 have been amended as requested by Applicant in Paper No. 20, filed March 19, 2002.

Claims 118-135 are withdrawn as being drawn to a non-elected invention.

Claims 24-117, 136-159 and 285-305 are currently under examination.

Withdrawn Rejections

2. The rejections of claims under 35 USC § 101 and § 112 are withdrawn in view of Applicants' amendment, and the statement concerning the availability of the deposited plasmid on page 10.

Information Disclosure Statement

3. Copies of initialed information disclosure statements, Paper Nos. 11, 15 and 21 are attached.

Drawings

4. The corrected or substitute drawings were received on March 19, 2002. These drawings are acceptable.

Claim Objections

5.1 Claim 301 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 301 is not further limiting because it encompasses the isolated polynucleotide of claim 286 which is DNA or RNA, and the polynucleotide of claim 286 has be either DNA or RNA.

5.2 Claims 31, 47, 64, 79, 95 and 109 are objected to because of the following informalities: they encompass a nucleic acid molecule that comprises or encodes a heterologous sequence. It would clarify the claims is the word "further" were inserted before comprises or comprising in claims 31, 47, 79, 95 and 109 and before the word "encodes" in claim 64.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6.1 Claims 136, 137, 148 and 149 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid molecule that encodes a polypeptide comprising at least amino acids 49-193 of SEQ ID NO: 2 and that binds Fas ligand, does not reasonably provide enablement for a nucleic acid molecule encoding at least 30 or 50 contiguous amino acids of SEQ ID NO: 2, wherein a protein consisting of said contiguous amino acids binds

Fas ligand. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The specification on pages 23 and 24 states that polypeptides having N-terminal deletions including the C49 residue in SEQ ID NO: 2 and C-terminal deletions including the cysteine at position 193 would not be expected to retain biological activity, because it is known that these residues in a TNFR-related polypeptide are required for forming a disulfide bridge to provide structural stability which is needed for receptor binding. Therefore, the minimal length of a polypeptide that would bind Fas ligand would be 145 amino acids in length. However, the claims encompass polypeptides 30 or 50 amino acids in length that would bind Fas ligand. Even though the claims recite "at least 30 (50) contiguous amino acids", there is a very significant difference between 30 or 50 amino acids and 145 amino acids, as far as Fas ligand binding is concerned. Therefore, the claims are not enabled for the claimed scope of the invention.

6.2 Claims 289-292 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polynucleotide comprising a nucleotide sequence of SEQ ID NO: 1 or a nucleotide sequence that encodes the polypeptide of SEQ ID NO: 2, does not reasonably provide enablement for polynucleotides that have 90 or 95% identity to those sequences. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant specification discloses a nucleic acid sequence of SEQ ID NO: 1 that encodes a polypeptide having the amino acid sequence of SEQ ID NO: 2 that has the activity of binding Fas ligand. However, the claims encompass nucleic acids encoding polypeptides that differ from

that of SEQ ID NO: 2. The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. While Applicants have provided some guidance as to possible amino acid residues that are not tolerant to change (alignments in Fig. 3), there is no limitation in the claims that the nucleic acids encode polypeptides that bind Fas ligand, the specification has not taught how to use polypeptides that do not bind Fas ligand. Adding the claim limitation that an encoded polypeptide binds Fas ligand would obviate the rejection.

6.3 Claims 289-292 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant disclosure of a single polypeptide, that of SEQ ID NO: 2 with the instantly disclosed specific activities, does not adequately support the scope of the claimed genus, which encompasses a substantial variety of subgenera. A genus claim may be supported by a representative number of species as set forth in *Regents of the University of California v Eli Lilly & Co,* 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), which states:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention". Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1980) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d 1565, 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id at 1170, 25 USPQ2d at 1606."

A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. The instant specification discloses, however, a single isolated polypeptide sequence SEQ ID NO: 2). Given the unpredictability of amino acid substitutions, deletions or additions, and the fact that the specification fails to provide objective evidence that the additional sequences are indeed species of the claimed genus it cannot be established that a representative number of species have been disclosed to support the genus claim. No activity is set forth for the additional sequences. The instantly claimed genus is not so limited and the prior

art does not provide compensatory structural or correlative teachings to enable one of skill to identify the polynucleotides encompassed. Adding the claim limitation that an encoded polypeptide binds Fas ligand would obviate the rejection.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 288, 289, 290, 298 and 302-305 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7.1 Claims 288, dependent claim 298, and claims 289 and 290 are indefinite because claims 288, 289 and 290 recite the isolated polynucleotide or nucleotide sequence "contained" in SEQ ID NO: 1, and it is not clear from this term if the entire sequence of SEQ ID NO: 1 is being claimed or only the region encoding SEQ ID NO: 2.

7.2 Claims 302-305 are indefinite because claim 302 has a misplaced modifier. It is suggested that the phrase "when said expression vector is present in a compatible host cell" be inserted after "SEQ ID NO: 2".

Conclusion

8.1 Claims 24-30, 32-46, 48-63, 65-78, 80-94, 96-108, 110-117, 138-147, 150-159, 285-287, 293-297, 299 and 300 are allowed.

8.2 Claims 136, 137, 148, 149, 288-292, 298 and 302-305 are rejected.

8.3 Claims 31, 47, 64, 79, 95, 109 and 301 are objected to.

8.4 Claims to non-elected inventions (118-135) should be canceled in response to this Office Action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (703) 308-3312. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

Official papers Before Final filed by RightFax should be directed to (703) 872-9306.

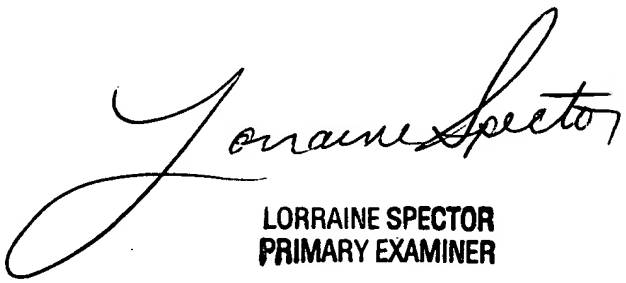
Official papers After Final filed by RightFax should be directed to (703) 872-9307.

Official papers filed by fax should be directed to (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Eileen B. O'Hara, Ph.D.

Patent Examiner



LORRAINE SPECTOR
PRIMARY EXAMINER